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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/936,888	BRENNEMAN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/28/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to comply*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on November 23, 2009 is acknowledged.

Claims 1-21, 34 and 35 are pending in the instant patent application.

Claims 1-21, 34 and 35 are under examination in the instant office action.

Sequence compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no computer readable form (CRF) copy of a "Sequence Listing" has been submitted in the instant patent application, see Notice to comply attached to the instant office action.

3. Further, no sequence identification has been provided for the amino acid sequences presented at p. 9 of the instant specification. In case these sequences are new, Applicant needs to provide a substitute paper copy of "Sequence Listing", a corresponding CRF and an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:)

be made in the specification and claims wherever a reference is made to that sequence. See MPEP 2422.04.

Claim Objections

4. Claims 1-21, 34 and 35 are objected to because of the following informalities: The claims recite "ADNF" without first providing the full name of the term. It is suggested that the term be spelled out at its first use and in all independent claims so that it is clearly understood what it stands for. Appropriate correction is suggested.

5. Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 16 depends from claim 2, which is limited to polypeptides, while claim 16 encompasses nucleic acids encoding those polypeptides. Therefore, claim 16 can be infringed by a nucleic acid, which does not infringe claim 2. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the nucleic acid claim could be infringed without infringing the claims from which it depends. Therefore, it is improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3, 4, 7, 8, 11, 12, 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 3, 4, 7, 8, 11, 12, 15 are vague and indefinite in so far as they employ the term "ADNF I" and "ADNF III" as limitations. This term, when coupled with reference to a full length of polypeptides or to their N- or C- terminus of the active core site but without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: does not allow one to determine the metes and bounds of "ADNF I" and "ADNF III". Therefore, an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of these limitations.

9. Claims 7, 11 and 15 are vague and indefinite in their recitation of limitation "up to about 20 amino acids". Although the term "about" in a claim is inherently vague and indefinite, its use is appropriate when employed to limit a value, which is composed of indefinitely divisible units such as inches, meters and grams where it is impractical to produce an item which has exactly the dimension recited. Even if one could practically produce an item, which is exactly 1 inch in length, the length of that item is conditional upon the temperature at which it is measured. However, when defining an invention in terms of indivisible numerical units such as the number of nucleotides in a nucleic acid, the number of amino acids in a polypeptide or the number of legs on a chair or table, the term "about" is unacceptably vague and indefinite since it is practical

to employ a term, which possesses the required precision. If, for example, it is Applicant's intension that the claims should encompass a polypeptide of more than a certain amount of amino acids in length then this is exactly what the claim should recite. Whereas one would reasonably interpret the term "about one inch" as encompassing any value from 0.90 inches to 1.10 inches one would not know if the term "up to about 20 amino acids" would exclude 19 or 21 amino acids.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 16-21, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for reducing a condition associated with fetal alcohol syndrome (FAS) in a subject who is exposed to alcohol *in utero*, the method comprising administration of an ADNF I polypeptide comprising the amino acid sequence of SEQ ID NO: 1, or an ADNF III polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or a mixture of ADNF I and ADNF III, does not reasonably provide enablement for the full scope of methods, such as administration of any ADNF polypeptide or nucleic acids encoding ADNF polypeptides as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 1, 16-21, 34 and 35 are directed to methods for reducing a condition associated with FAS by administration of ADNF polypeptides or nucleic acids encoding ADNF polypeptides to the fetus *in utero* or to the pregnant female who has been consuming alcohol

prior to the treatment. However, the specification fails to enable one in the art how to practice the claimed invention. The specification fails to set forth sufficient guidance to one in the art, thus, requiring undue experimentation on part of a skilled artisan to discover how to use Applicant's method, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The instant specification discloses results of series of experiments on mice, in which the animals were treated with ADNF I or/and ADNF III prior to administration of ethyl alcohol or as a post-treatment, see pp. 42-50. The results indicated that several parameters associated with FAS were improved or reduced. However, the specification fails to present any factual evidence or supply a line of scientific reasoning to support the full scope of the instant claimed methods, such as administration of any polypeptide broadly recited as ADNF or practicing gene therapy methods and administering nucleic acids to pregnant females or directly to the fetus.

The instant specification provides no disclosure or working examples on how to use nucleic acid molecules encoding ADNF polypeptide(s) for gene therapy applications, such as for treatment of FAS. The state of the art at the time of filing clearly recognizes the high level of unpredictability of any, *in vivo* or *ex vivo*, gene delivery procedures. For example, article by Welsh (Welsh, 1999, Current Opinion in Mol. Therapeutics, 1 (4), pp. 464-470) provides a

review of advances in the development of clinically effective gene transfers. It is clear from the publication that at the time of invention the gene therapy approach remained not fully developed with respect to reliable and safe vector delivery systems and was considered risky and generally unpredictable (see p.464 and 467 specifically). Roth et al. provide similar explanation and concerns regarding technical challenges to deliver controlled, therapeutic levels of a gene to a particular cell type to obtain the desired clinical effect stating that "[t]he state of gene therapy was critically evaluated by the National Institute of Health in 1995 [...]. One of primary impediments to successful gene therapy was identified as the low frequency of gene transfer, resulting in insufficient therapeutic benefits" (Roth et al., 1999, Ann. Rev. Biomed. Eng., 01, pp.265-297, specifically page 283).

"[T]o be enabling, the specification.., must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Wright*, 999 F.2d at 1561, 27 USPQ2d at 1513 (emphasis added), quoted in *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997). Thus, "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23, 20 USPQ2d 1438, 1445 & n. 23 (Fed. Cir. 1991), quoted in *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1372, 52 USPQ2d 1129, 1138 (Fed. Cir. 1999).

"Patent protection is granted in return for an enabling disclosure..., not for vague intimations of general ideas that may or may not be workable." *Genentech*, 108 F.3d at 1365, 42 USPQ2d at 1005. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or

exemplified in the specification, reasonable detail must be provided in order to enable members of the public [skilled in the art] to understand and carry out the invention." *Id.* at 1366, 42 USPQ2d at 1005 (emphasis added).

Therefore, in view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for methods of treatment by administration of any ADNF polypeptide or an isolated nucleic acid molecule encoding an ADNF polypeptide to the fetus. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicant's invention as currently claimed.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-15, 17-21, 34 and 35 are rejected on the ground of nonstatutory double patenting over claims 116 of U. S. Patent No. 6,933,277 (henceforth referred to as '277 patent) since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: claims 1-16 of the '277 patent fully teach the enabled scope of the instant claimed method and therefore fully anticipate claims 1-15, 17-21, 34 and 35.

14. It is noted that Applicant has filed multiple patent applications directed to common steps of administration of ADNF polypeptides - 12/197,915; 12/102,760; 12/197,986, for example. Because of Applicant's prolific Patent and Application portfolio, the burden is shifted to Applicant to identify all relevant Applications and Patents and to include said Applications and Patents on any terminal disclaimer filed.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Olga N. Chernyshev/
Primary Examiner, Art Unit 1649

January 25, 2010